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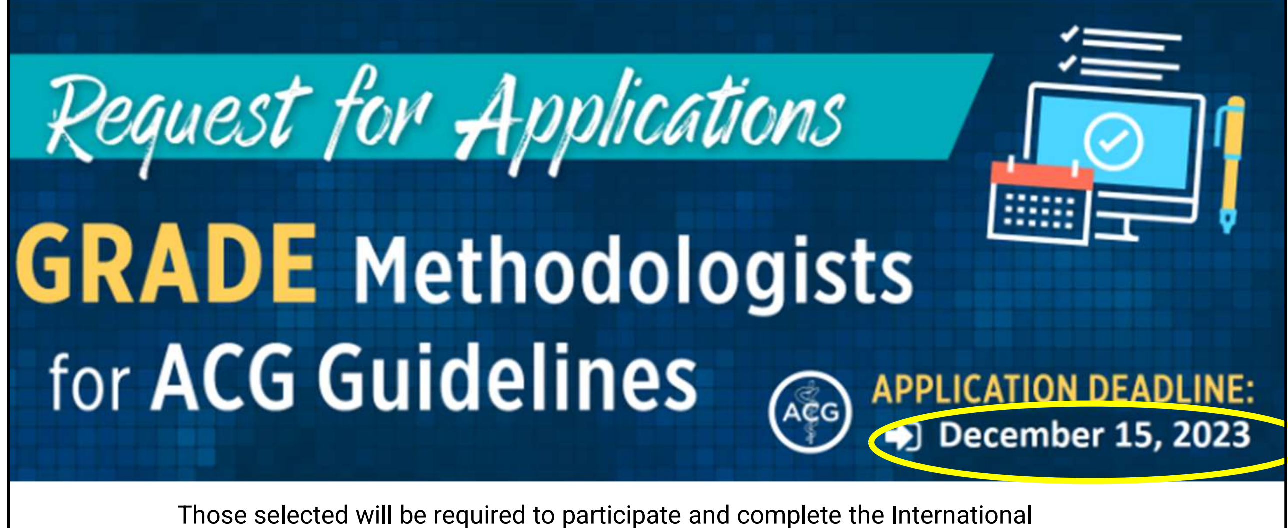

Those selected will be required to participate and complete the International Guideline Development Credentialing & Certification Program through McMaster University. The onsite training will be in Spring 2024 and is sponsored by the ACG. Applicants must agree to a 5-year term as a GRADE Methodologist.

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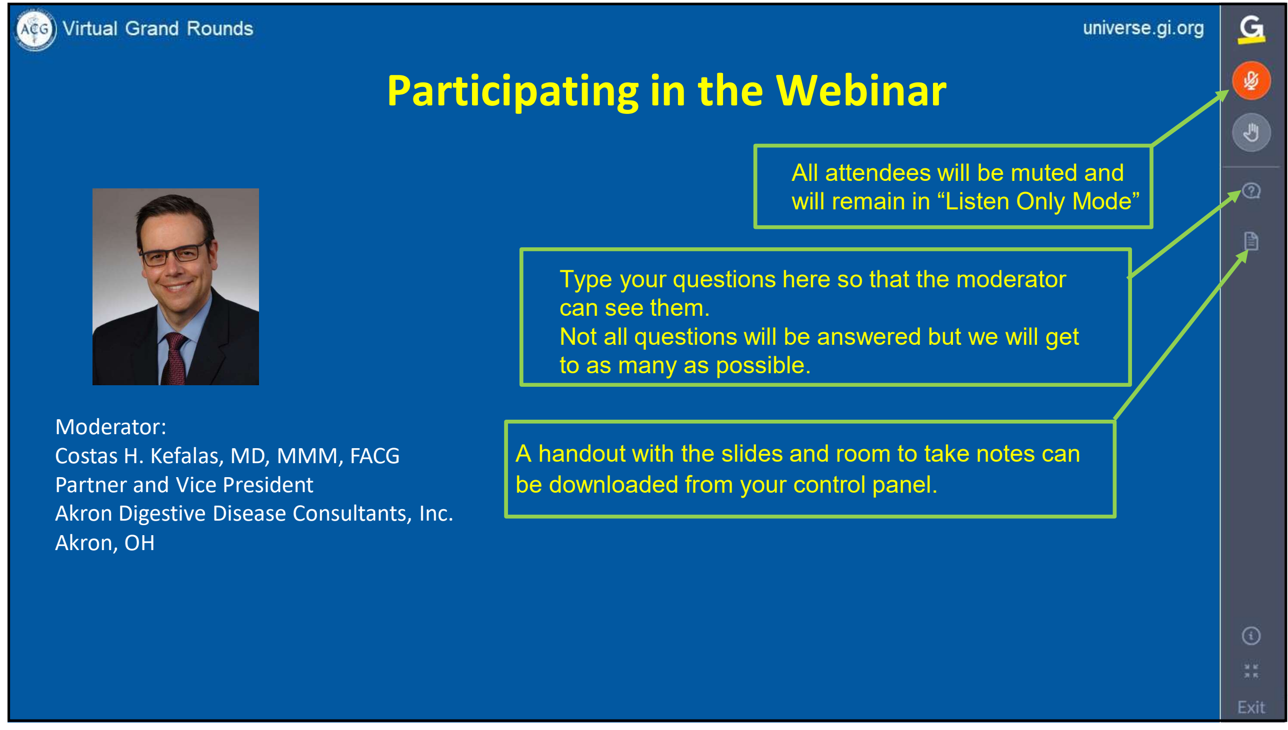

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ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 2 – Thursday, January 11, 2024
Evidence-Based GI Highlights: Advances in IBD Therapy
Faculty: Bharati Kochar, MD, MS
Moderator: Philip S Schoenfeld, MD, MSEd, MSCEPi, FACG
At Noon and 8pm Eastern

Week 3 – Thursday, January 18, 2024
Joy and Wellness in Gastroenterology
Faculty: Richard S. Bloomfeld, MD FACG
Moderator: Jonathan A. Leighton, MD, FACG
At Noon and 8pm Eastern

Visit **gi.org/ACGVGR** to Register

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Antibiotic Stewardship:

Appropriate Use in Common GI Scenarios

A case-based review of the ACG guidelines

Neil Stollman, MD, FACG

Chief, Division of Gastroenterology, Alta Bates Summit Medical Center, Oakland, CA

Associate Clinical Professor of Medicine, UCSF

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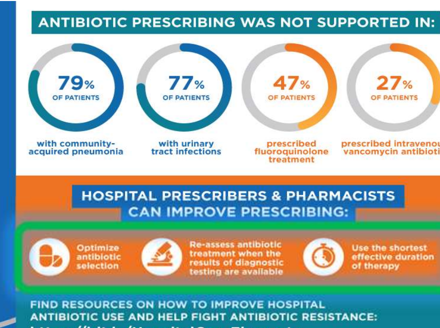
SELECTIVE USE IS KEY

- Abx overused (~50%) and cause AEs (~20% of ER visits d/t Abx AEs)
- White House & CDC: $1.2B National Strategy to Combat Antibiotic Resistance
- Could some patients typically given antibiotics be safely treated without?



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Antibiotic Rx best practices in:

- ❖ *C difficile* infection
- ❖ Acute diverticulitis
- ❖ Acute pancreatitis
- ❖ Ischemic colitis
- ❖ Acute diarrheal infections

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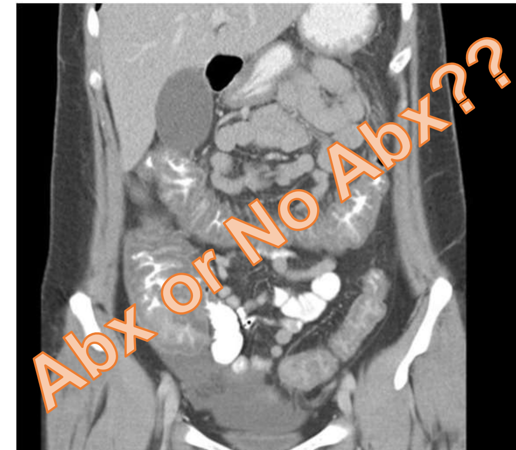
Case #1

- 78 year-old woman presents to the ER with weakness, confusion, fevers, diarrhea. S/P 7d ciprofloxacin for UTI, last dose 3 days ago
- No prior GI hx except GERD
- Temp 100.9, BP 102/78, HR 110
- PEx: mild diffuse abd TTP, no R/G
- WBC 22K, others WNL
- CT A/P with extensive colonic submucosal edema
- ER activating sepsis protocol and plan broad spectrum abx, but call GI consult too



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Current Guidelines (ACG 2021): Prevention of *C difficile*

- Antibiotic stewardship (quinolones, clindamycin worst)
- Isolation when available; continue 48h after diarrhea resolves
- Hand Hygiene / Contact Precautions (gloves and gowns)
- "Moderate evidence" that probiotics (particularly *Lactobacillus GG* and *Saccharomyces boulardii*) diminish antibiotic associated diarrhea, but do not recommend their routine use for prevention of infection or recurrence.
- Discontinue unnecessary PPIs (but don't stop if appropriate)

Kelly CR, et al. Am J Gastroenterol. 2021

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Anti-CDI Antibiotics

Metronidazole
Very inexpensive
(<$10)

Vancomycin
$150 for 10 day course

Fidaxomicin
$4400 for 10 day course

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Non-Severe: Initial Episode

- Stop offending antibiotics if possible
- Avoid anti-peristaltic agents
- Empiric Rx appropriate when high suspicion

Vancomycin 125 mg PO QID x 10d
Strong recommendation, low quality of evidence

Or

Fidaxomicin 200 mg PO BID x 10d

Metronidazole 500 mg PO TID x 10 days may be considered for initial treatment in low-risk patients (young, outpatient, no comorbidities)
Strong recommendation, moderate quality of evidence

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Severe: Initial Episode

Vancomycin 125 mg PO QID x 10 days

Strong recommendation, low quality of evidence

Or

Fidaxomicin 200 mg PO BID x 10 days

Conditional recommendation, very low quality of evidence

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Fulminant Infection

- Volume resuscitation, early surgical consultation, imaging for ileus, megacolon
- **Vancomycin** 500 mg PO Q6h for the first 48-72 hours
  - *Strong recommendation, very low quality of evidence*
- and **Metronidazole** 500 mg IV Q8h
- (especially beneficial with paralytic ileus)
  - *Conditional recommendation, very low quality of evidence*
- Ileus: The addition of vancomycin enemas (500 mg Q6h) may be beneficial.
  - *Conditional recommendation, very low quality of evidence*
- **Consider FMT if no response in 48h (data favorable)**

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Treatment of Recurrent Infection

- Fidaxomicin for patients experiencing a first recurrence after an initial course of vancomycin or metronidazole
  - *Strong recommendation, moderate quality of evidence*
- OR tapering/pulsed-dose vancomycin for patients experiencing a first recurrence after an initial course of fidaxomicin, vanco or metronidazole
  - *Strong recommendation, very low quality of evidence*
- Bezlotoximab*:* "We suggest bezlotoxumab be considered for prevention of CDI recurrence in patients who are at high risk of recurrence (age >65 and immunocompromised suggested)
  - *conditional recommendation, moderate quality of evidence*
  - *Note: cardiac contraindication*

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Suppressive and Prophylactic Vancomycin

- For patients with rCDI who are not candidates for FMT, who relapsed after FMT, or who require ongoing or frequent courses of antibiotics, long-term suppressive oral vancomycin may be used to prevent further recurrences (125mg PO QD-TID)
  - *Conditional recommendation, very low quality of evidence*
- Oral vancomycin prophylaxis (OVP) may be considered during subsequent systemic antibiotic use in patients with a history of CDI who are at high risk of recurrence to prevent further recurrence
  - *Conditional recommendation, low quality of evidence*
  - *Trial ongoing*

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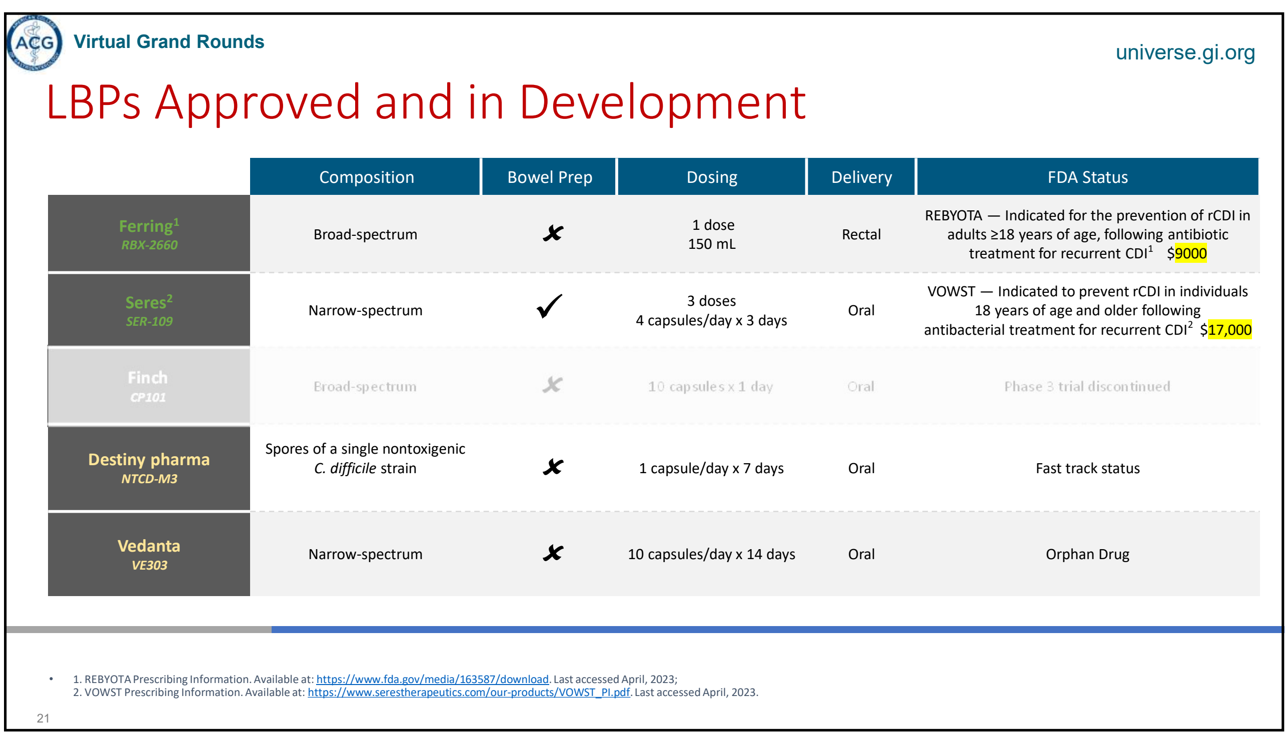

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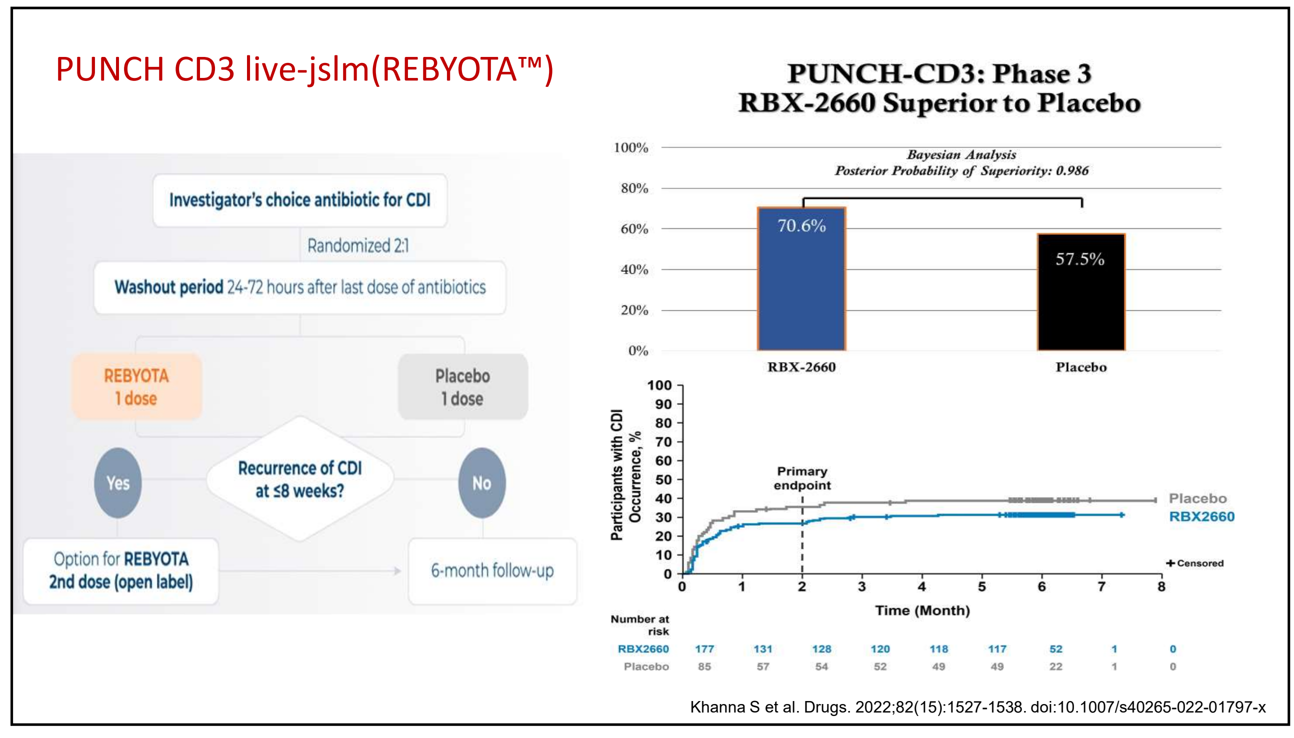

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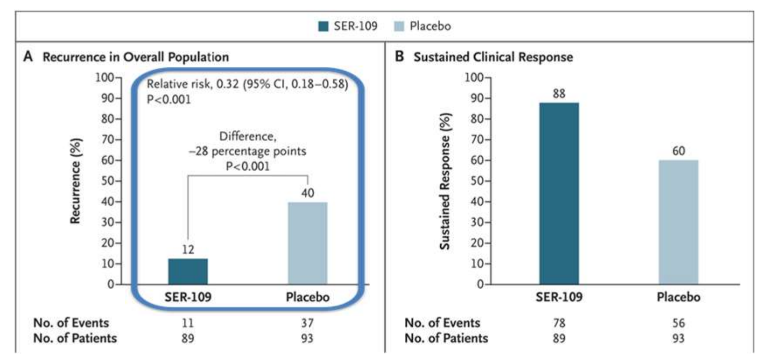
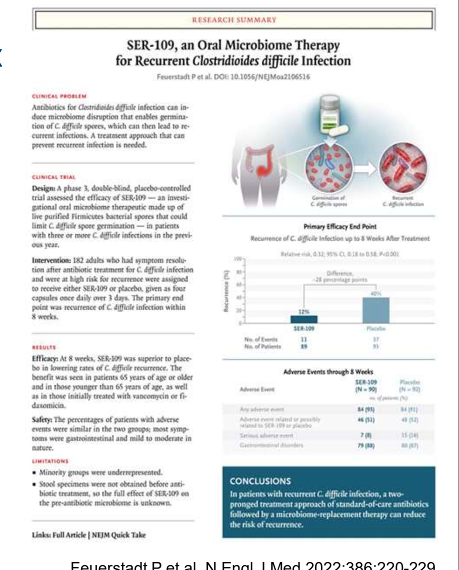
SER 109 ECOSPOR (VOWST™)

- Live purified *Firmicutes* spores
- 182 pts with >3 CDIs / one year, responsive to Abx
- 4 capsules/d x3d vs PBO after vanco or fidax
- Primary outcome rCDI at 8 weeks





RESEARCH SUMMARY

SER-109, an Oral Microbiome Therapy for Recurrent *Clostridioides difficile* Infection

Feuerstadt P et al. DOI: 10.1056/NEJMoa2106516

CLINICAL PROBLEM

Antibiotics for *Clostridioides difficile* infection can induce microbiome disruption that enables germination of *C. difficile* spores, which can then lead to recurrent infections. A treatment approach that can prevent recurrent infection is needed.

CLINICAL TRIAL

Design: A phase 3, double-blind, placebo-controlled trial assessed the efficacy of SER-109 — an investigational oral microbiome therapeutic made up of live purified Firmicutes bacterial spores that could limit *C. difficile* spore germination — in patients with three or more *C. difficile* infections in the previous year.

Intervention: 182 adults who had symptom resolution after antibiotic treatment for *C. difficile* infection and were at high risk for recurrence were assigned to receive either SER-109 or placebo, given as four capsules once daily over 3 days. The primary end point was recurrence of *C. difficile* infection within 8 weeks.

RESULTS

Efficacy: At 8 weeks, SER-109 was superior to placebo in lowering rates of *C. difficile* recurrence. The benefit was seen in patients 65 years of age or older and in those younger than 65 years of age, as well as in those initially treated with vancomycin or fidaxomicin.

Safety: The percentages of patients with adverse events were similar in the two groups; most symptoms were gastrointestinal and mild to moderate in nature.

LIMITATIONS

- Minority groups were underrepresented.
- Stool specimens were not obtained before antibiotic treatment, so the full effect of SER-109 on the pre-antibiotic microbiome is unknown.

Links: Full Article | NEJM Quick Take

Germination of *C. difficile* spores
Recurrent *C. difficile* infection

Primary Efficacy End Point

Recurrence of *C. difficile* Infection up to 8 Weeks After Treatment

Relative risk, 0.32; 95% CI, 0.18 to 0.58; P<0.001

Difference, −28 percentage points

	SER-109	Placebo
Recurrence	12%	40%
No. of Events	11	37
No. of Patients	89	93

Adverse Events through 8 Weeks

Adverse Event	SER-109 (N = 90)	Placebo (N = 92)
	no. of patients (%)	
Any adverse event	84 (93)	84 (91)
Adverse event related or possibly related to SER-109 or placebo	46 (51)	48 (52)
Serious adverse event	7 (8)	15 (16)
Gastrointestinal disorders	79 (88)	80 (87)

CONCLUSIONS

In patients with recurrent *C. difficile* infection, a two-pronged treatment approach of standard-of-care antibiotics followed by a microbiome-replacement therapy can reduce the risk of recurrence.

Feuerstadt P et al. N Engl J Med 2022;386:220-229

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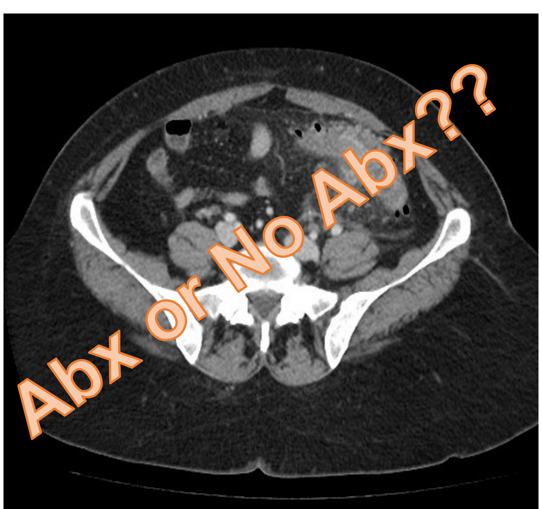
Case #2

- 48-year-old attorney presents to the ER with 2 days of worsening LLQ pain and feeling feverish
- No prior GI hx or colonoscopy
- BMI 36, Temp 100.2, BP 122/78, HR 96
- PEx: mild TTP LLQ, no R/G
- WBC 12K, others WNL
- CT A/P with diverticula, wall thickening sigmoid and mesenteric stranding
- Candidate for outpatient Rx per ER MD



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Who says use Abx in AD? (hint: everyone)

- ***ACG Practice Guidelines 1999:*** "Selected patients with mild diverticulitis can be treated as outpatients with broad-spectrum oral antibiotics. Patients with more severe illness or comorbid disease should be hospitalized and treated with bowel rest & IV antibiotics".
- ***IDSA Guidelines 2010****: "*For acute diverticulitis…..regimens for treatment of mild-to-moderate severity infection are recommended, with a possibility of early oral therapy"
- ***Medscape 2016:*** "Antibiotics are used for ***every*** stage of diverticulitis. Empiric therapy requires broad-spectrum antibiotics……"
- ***WebMD 2016:*** "treated with medicines such as antibiotics…."
- ***Merck Manual 2016:*** "Treatment varies with severity. Liquid diet, oral antibiotics for mild disease and IV antibiotics for severe…."
- ***UpToDate 2016:*** "The outpatient treatment of acute colonic diverticulitis typically consists of oral antibiotics and a limited diet for 7 to 10 days"

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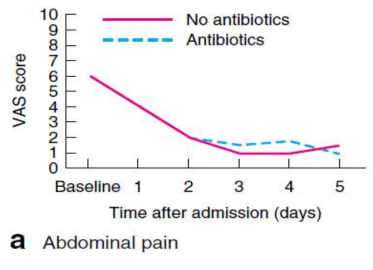
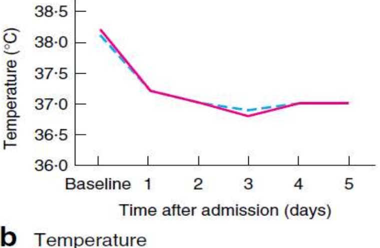
AVOD: Swedish RCT, 623 pts, unblinded

CT-confirmed AUD, **No** Abx vs Abx for ≥ 7 days at MD's discretion

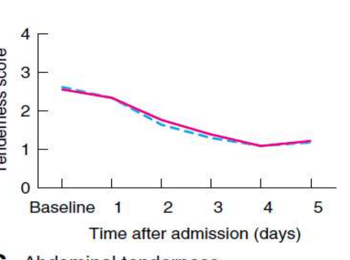
	Abscess, perforation (*P* = 0.3)	**Recurrent diverticulitis (*P* = 0.88)**
No antibiotics	6 (1.9%)	47 (16.2%)
Antibiotics	3 (1.0%)	46 (15.8%)



a Abdominal pain

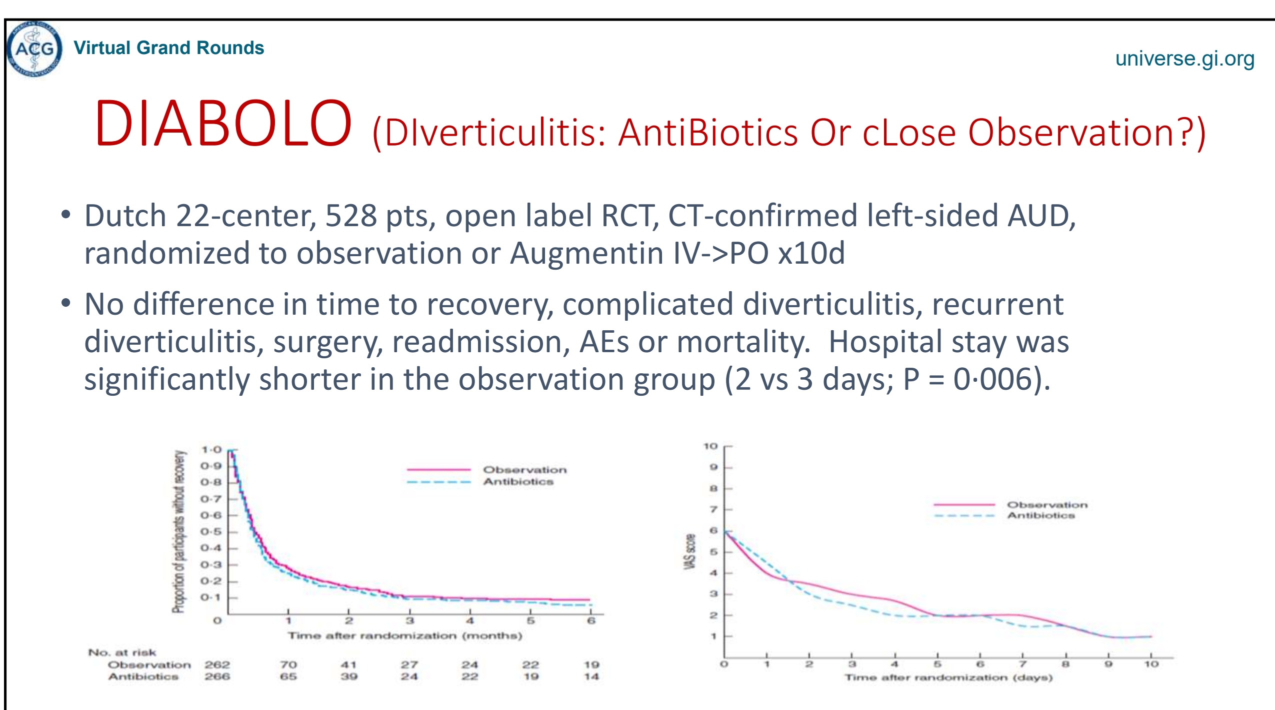


b Temperature



c Abdominal tenderness

Chabok A et al. British Journal of Surgery 2012;99:532.



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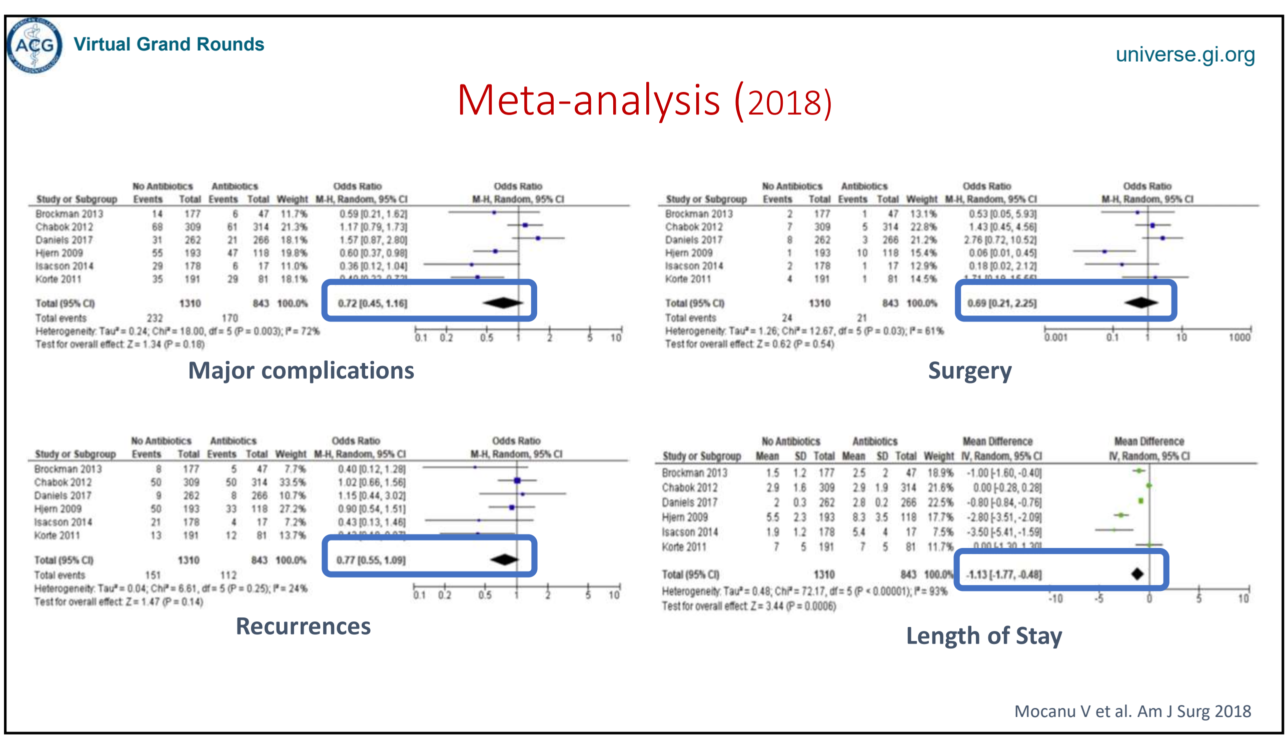

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AGA Practice Guidelines (2015)

Question 1. Should Antibiotics Be Routinely Used in Patients With Acute Uncomplicated Diverticulitis?

The AGA suggests that antibiotics should be used selectively, rather than routinely, in patients with acute uncomplicated diverticulitis. (*Conditional recommendation, low quality of evidence*).

Observation possible in pts without severe comorbidities and no abscess or other complications

Stollman N et al. AGA Guideline on the Management of Acute Diverticulitis. Gastroenterology. 2015 Dec;149(7):1944-9.

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AGA CPU (2021)

- Antibiotic treatment can be used ***selectively***, rather than routinely, in **immunocompetent patients with mild uncomplicated diverticulitis.**
- Antibiotic Rx is advised in pts with complicated diverticulitis or uncomplicated disease with comorbidities or are frail, who present with refractory symptoms or have a CRP >140 mg/L or WBC > 15K

Peery AF et al. Gastroenterology 2021;160:906-911.

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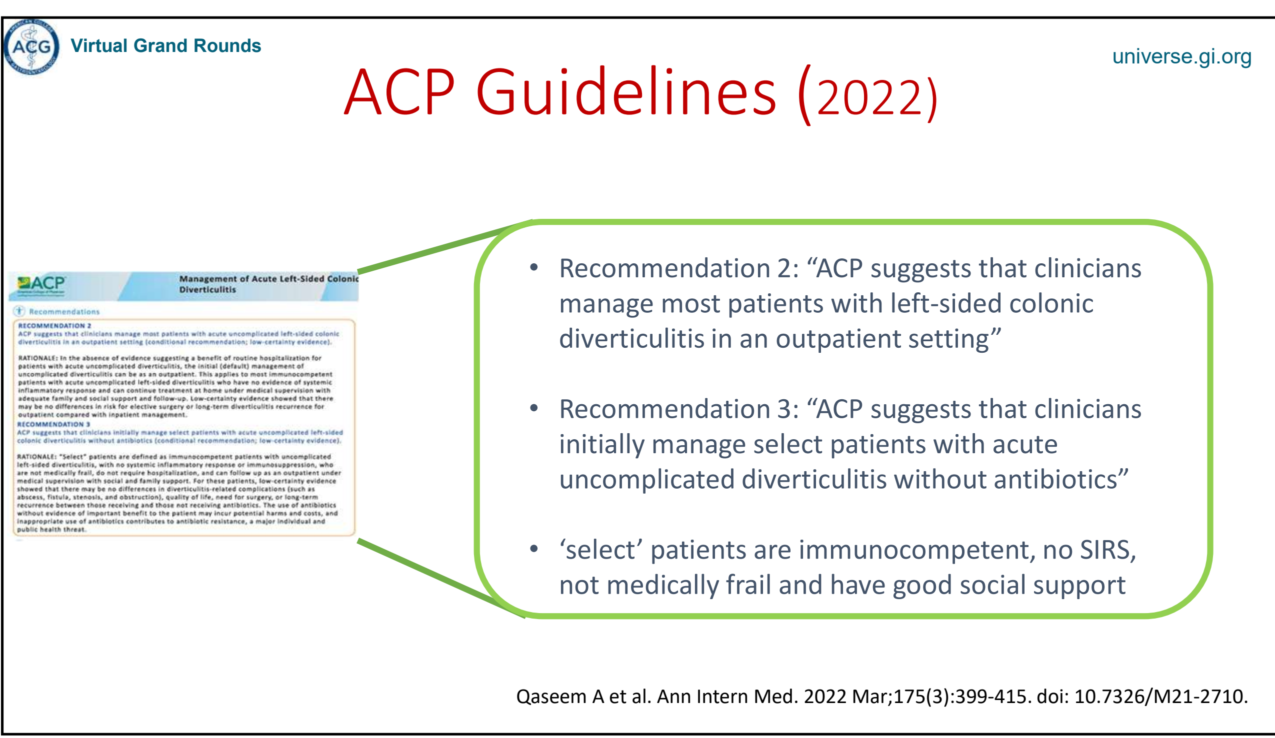

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Bonus: other key diverticulitis guidelines pearls

- AVOID repetitive NSAIDs
- Increased exercise and high fiber diets lower recurrences
- Colonoscopy after resolution if 'adequate exam not recently done' (especially in complicated diverticulitis)
- Surgery now individualized (prior after 'second attack', now later)
- Seeds and nuts: OK!
- No data supported role for mesalamine, rifaximin, probiotics

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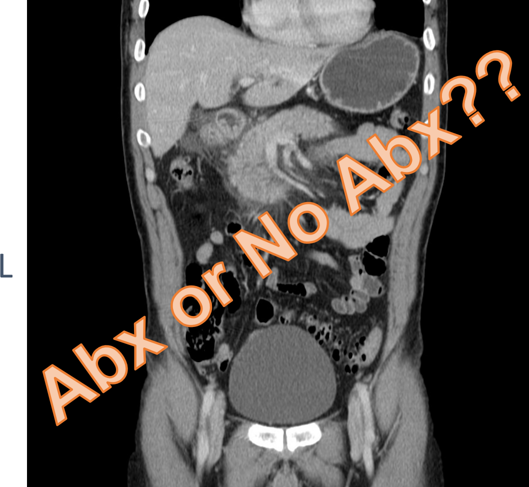
Case #3

- 48-year-old attorney presents to the ER with 2 days of worsening mid abd pain -> back, nausea and vomiting
- Prior CCx, nightly cocktails (and more on recent vacation)
- BMI 24, Temp 100.8, BP 122/78, HR 96, RR 16, O2 sat 98% RA
- PEx: mod mid abd TTP, +guarding
- WBC 12K, Hct 49%, lipase 1288, others WNL
- CT A/P with diffuse enhancement, peri-pancreatic fat stranding and peri-duodenal fluid, no necrosis
- Admitted general floor for IVF, pain control



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Preventing (& treating) infection in AP

- Infection much less common in non-necrotizing AP ('interstitial' or 'edematous') (and this patient has mild AP)
- Concern re necrosis if persisting / worsening 7-10d (Dx by CT)
- Logical to consider if empiric prophylactic Abx could PREVENT infection in patients with necrosis: trials negative and NNT > 1000
- Abx appropriate with documented *infected* necrosis (but recall many abx don't achieve tissue levels in pancreatic necrosis)

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ACG Guidelines (2013)

- Treat extra-pancreatic infections as appropriate
- **No** routine use of prophylactic Abx in severe AP
- **No** routine use of Abx to prevent infected necrosis
- When concerned re infected necrosis (deterioration or failure to improve after 7-10d) either CT FNA and Gram stain and Cx to guide Abx OR empiric Abx
- In patients with infected necrosis, use Abx known to penetrate (carbapenems, quinolones, metronidazole)
- Routine antifungal Rx NOT recommended

THE ROLE OF ANTIBIOTICS IN AP

Recommendations

1. Antibiotics should be given for an extrapancreatic infection, such as cholangitis, catheter-acquired infections, bacteremia, urinary tract infections, pneumonia (strong recommendation, moderate quality of evidence).
2. Routine use of prophylactic antibiotics in patients with severe AP is not recommended (strong recommendation, moderate quality of evidence).
3. The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is not recommended (strong recommendation, moderate quality of evidence).
4. Infected necrosis should be considered in patients with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7–10 days of hospitalization. In these patients, either (i) initial CT-guided fine-needle aspiration (FNA) for Gram stain and culture to guide use of appropriate antibiotics or (ii) empiric use of antibiotics after obtaining necessary cultures for infectious agents, without CT FNA, should be given (strong recommendation, moderate evidence).
5. In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis, such as carbapenems, quinolones, and metronidazole, may be useful in delaying or sometimes totally avoiding intervention, thus decreasing morbidity and mortality (conditional recommendation, moderate quality of evidence).
6. Routine administration of antifungal agents along with prophylactic or therapeutic antibiotics is not recommended (conditional recommendation, low quality of evidence).

Tenner S et al. American Journal of Gastroenterology 2013; 108: 1400-1415 doi: 10.1038/ajg.2013.218

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AGA Guidelines (2018)

Recommendation 2. In patients with predicted severe AP and necrotizing pancreatitis, the AGA suggests against the use of prophylactic antibiotics. *Conditional recommendation, low quality evidence.*

(Clarified explicitly that it also applied to mild disease)

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Bonus: other key pancreatitis guideline pearls

- Prior recs for aggressive hydration now questioned and ‘moderate’ hydration’ is recommended, most favor LR but not conclusive
- ERCP w/in 24h for acute cholangitis, hold if no biliary obstruction
- CCx during admission for biliary pancreatitis
- OK to feed mild AP if no pain or n/v. Low-fat solid diet as safe as clears (AGA: oral feeds w/in 24h if tolerated)
- ACG and AGA: strong preference ENTERAL over parental feeding and for both NG = NJ

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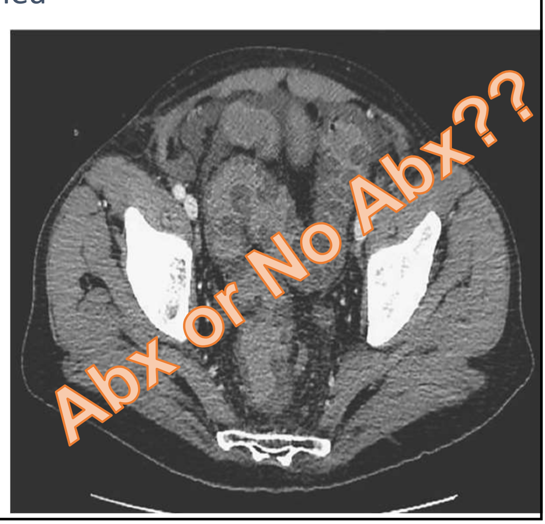
Case #4

- 78-year-old attorney presents to the ER with 2 days of abrupt onset of now worsening LLQ pain with bloody diarrhea
- Hx DMII, CAD
- BMI 26, Temp 100.8, BP 112/78, HR 116, RR 20, O2 sat 98% RA
- PEx: mod LLQ TTP, +guarding
- WBC 17K, Bun 44, Cr 1.4, rest WNL
- CT A/P sigmoid colon thickening with thumbprinting
- Admitted general floor for IVF, pain control



CT: D Manatakis. N Engl J Med 2018;378:e33.

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ACG Guidelines (2015)

- No high quality data on Abx in colonic ischemia
- "Antimicrobial therapy should be considered in patients with ***moderate*** or ***severe*** CI" (expert opinion)
- "…broad spectrum, including anaerobic coverage"
- "…at least 72 hours and 7-day course should be considered"

(strong recommendation, very low level of evidence)

Brandt L et al. Am J Gastroenterol 2015; 110:p18-44 doi: 10.1038/ajg.2014.395

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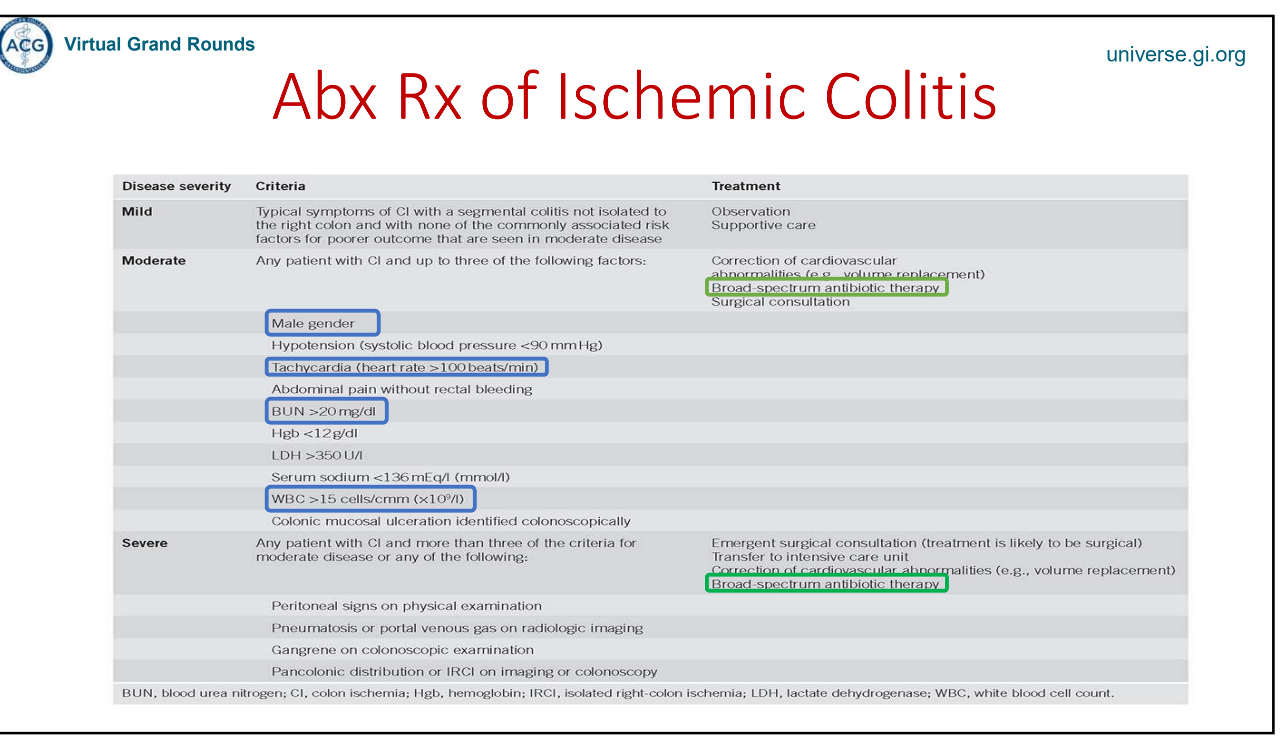
Abx Rx of Ischemic Colitis



Disease severity	Criteria	Treatment
Mild	Typical symptoms of CI with a segmental colitis not isolated to the right colon and with none of the commonly associated risk factors for poorer outcome that are seen in moderate disease	Observation Supportive care
Moderate	Any patient with CI and up to three of the following factors:	Correction of cardiovascular abnormalities (e.g., volume replacement) Broad-spectrum antibiotic therapy Surgical consultation
	Male gender	
	Hypotension (systolic blood pressure <90 mm Hg)	
	Tachycardia (heart rate >100 beats/min)	
	Abdominal pain without rectal bleeding	
	BUN >20 mg/dl	
	Hgb <12 g/dl	
	LDH >350 U/l	
	Serum sodium <136 mEq/l (mmol/l)	
	WBC >15 cells/cmm ($\times 10^9$/l)	
	Colonic mucosal ulceration identified colonoscopically	
Severe	Any patient with CI and more than three of the criteria for moderate disease or any of the following:	Emergent surgical consultation (treatment is likely to be surgical) Transfer to intensive care unit Correction of cardiovascular abnormalities (e.g., volume replacement) Broad-spectrum antibiotic therapy
	Peritoneal signs on physical examination	
	Pneumatosis or portal venous gas on radiologic imaging	
	Gangrene on colonoscopic examination	
	Pancolonic distribution or IRCI on imaging or colonoscopy	

BUN, blood urea nitrogen; CI, colon ischemia; Hgb, hemoglobin; IRCI, isolated right-colon ischemia; LDH, lactate dehydrogenase; WBC, white blood cell count.

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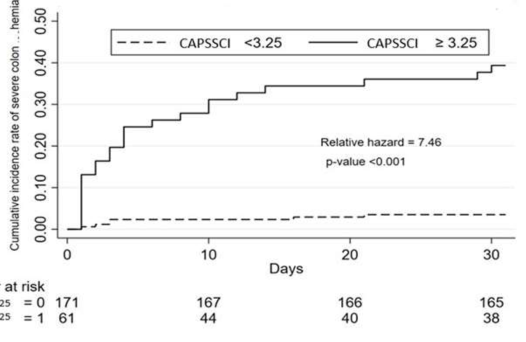
CAPSSCI

- CAPSSCI: risk score for IC including age, history of CAD,PVD, shock index, albumin level, and CT findings; no colonoscopy findings
- Score of < 3.25 = low risk for 30-day mortality and or colectomy
- Score of ≥ 3.25 = high risk for 30-day mortality and or colectomy



Oral Presentation ACG October 2023. Development of a Clinically Applicable Prognostication Severity Score for Colon Ischemia in Hospitalized Patients. Rizwan R, … Brandt, L.

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Bonus: other key colonic ischemia guideline pearls

- Most cases are mild and will resolve spontaneously but isolated right sided colonic ischemia (IRCI) has significantly worse prognosis
- Pneumatosis and portal venous gas predict infarction
- Colonoscopy (48h) in suspected disease, with minimal air insufflation, to assess extent of disease (and stop there after biopsies).
- No colonoscopy if gangrene, infarction (and consult surgery)

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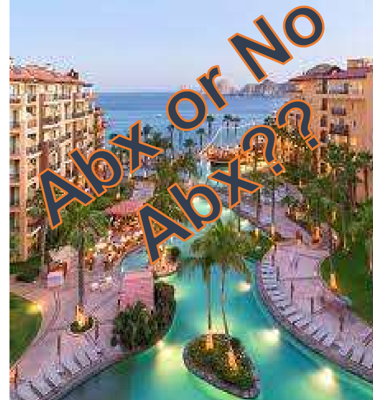
Case #5

- 58-year-old man vacation in Mexico with large group, many developed acute watery diarrhea, self Rx with pepto bismol with rapid resolution of Sxs in all, including patient, but a week later, he alone had recurrent severe watery diarrhea.
- No blood, no fevers. Abd cramps.
- Tolerating PO intake but feels weak
- Temp 98.8, BP 102/78, HR 110
- PEx: mild diffuse TTP w/o rebound/guarding
- Stool multiplex PCR ordered



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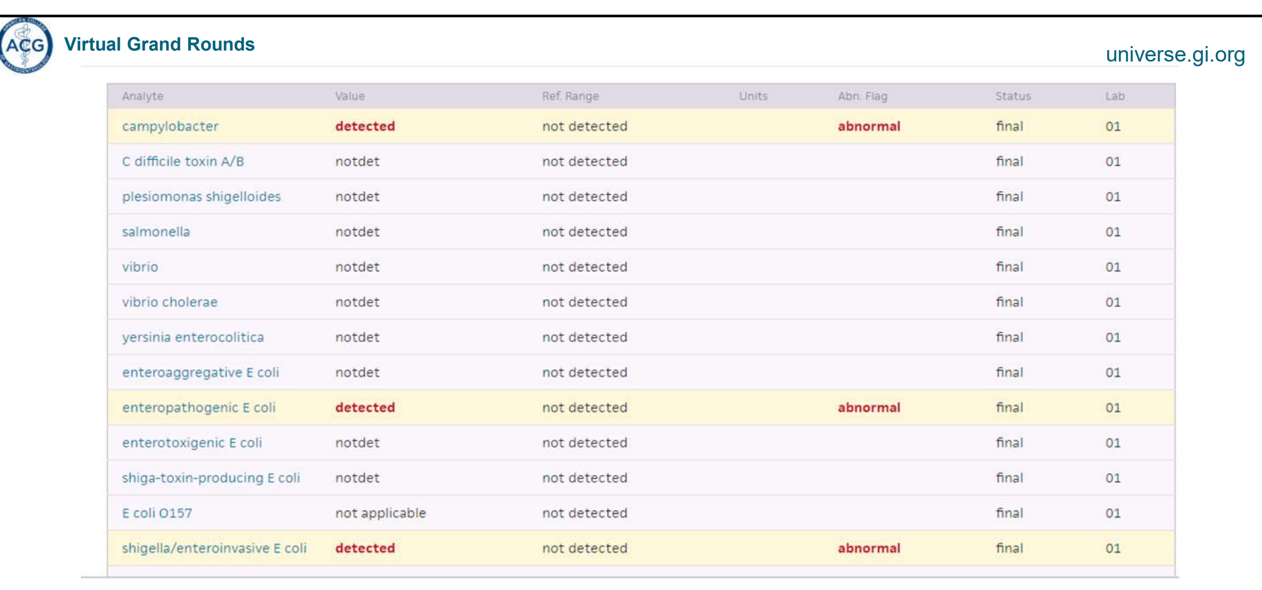

Analyte	Value	Ref. Range	Units	Abn. Flag	Status	Lab
campylobacter	detected	not detected		abnormal	final	01
C difficile toxin A/B	notdet	not detected			final	01
plesiomonas shigelloides	notdet	not detected			final	01
salmonella	notdet	not detected			final	01
vibrio	notdet	not detected			final	01
vibrio cholerae	notdet	not detected			final	01
yersinia enterocolitica	notdet	not detected			final	01
enteroaggregative E coli	notdet	not detected			final	01
enteropathogenic E coli	detected	not detected		abnormal	final	01
enterotoxigenic E coli	notdet	not detected			final	01
shiga-toxin-producing E coli	notdet	not detected			final	01
E coli O157	not applicable	not detected			final	01
shigella/enteroinvasive E coli	detected	not detected		abnormal	final	01

Was treated empirically with azithromycin 1gm x1 with impressive and rapid symptom resolution. Dept of Public Health investigated

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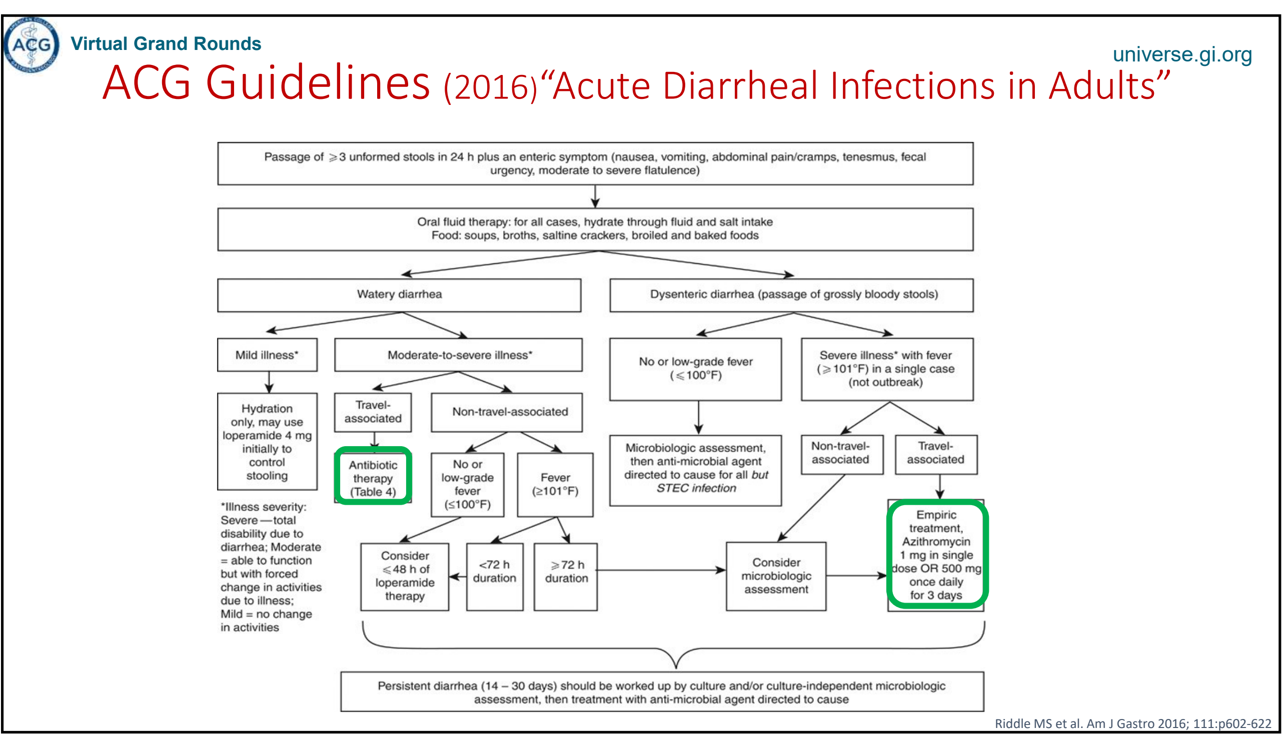

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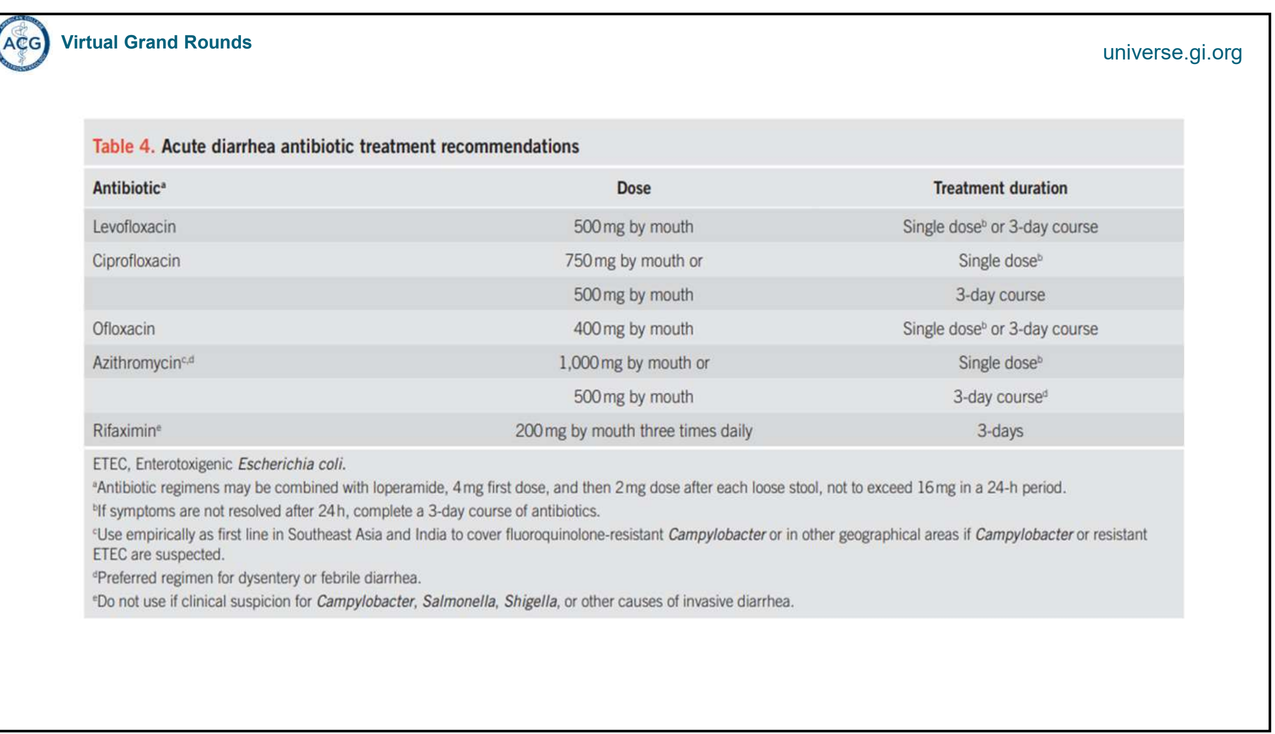

Table 4. Acute diarrhea antibiotic treatment recommendations

Antibiotic[a]	Dose	Treatment duration
Levofloxacin	500 mg by mouth	Single dose[b] or 3-day course
Ciprofloxacin	750 mg by mouth or	Single dose[b]
	500 mg by mouth	3-day course
Ofloxacin	400 mg by mouth	Single dose[b] or 3-day course
Azithromycin[c,d]	1,000 mg by mouth or	Single dose[b]
	500 mg by mouth	3-day course[d]
Rifaximin[e]	200 mg by mouth three times daily	3-days

ETEC, Enterotoxigenic *Escherichia coli*.
[a]Antibiotic regimens may be combined with loperamide, 4 mg first dose, and then 2 mg dose after each loose stool, not to exceed 16 mg in a 24-h period.
[b]If symptoms are not resolved after 24 h, complete a 3-day course of antibiotics.
[c]Use empirically as first line in Southeast Asia and India to cover fluoroquinolone-resistant *Campylobacter* or in other geographical areas if *Campylobacter* or resistant ETEC are suspected.
[d]Preferred regimen for dysentery or febrile diarrhea.
[e]Do not use if clinical suspicion for *Campylobacter*, *Salmonella*, *Shigella*, or other causes of invasive diarrhea.

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Bonus: other key acute diarrheal infection guideline pearls

- "Use of antibiotics for community-acquired diarrhea should be discouraged..(most are viral)"
- Non-culture (multiplex PCR) testing has many advantages, but suffers from poor specificity (sub-pathogenic levels) and no public health info
- Probiotics *not* recommended for prophylaxis or active Rx of TD
- Bismuth **is** recommended as both prophylaxis and active Rx
- OK to add loperamide to Abx treated patients
- Abx chemoprophylaxis has moderate effectiveness; consider in high-risk groups for short term use (undefined 'high risk')
  - Quinolones or rifaximin

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Appropriate Abx in GI: recap

- ❖CDI: vanco or fidax, then pulse/taper, then LBPs
- ❖It is appropriate to withhold antibiotics in select patients with acute uncomplicated diverticulitis
- ❖There is no role for empiric antibiotics (or antifungals) in acute pancreatitis absent infected necrosis
- ❖Empiric Abx indicated for moderate or severe colonic ischemia
- ❖Antibiotics for mod/severe traveler's diarrhea; culture (or PCR) if persistent, febrile, bloody

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